Case of the Month

Giant Multiple Intraductal Papilloma of the Breast: A Case Report and Review of the Literature

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Abstract

A case is described of multiple intraductal papilloma of the breast in a 39 year old Micronesian female who presented to our institution with a 2 year history of spontaneous bloody nipple discharge with an associated giant cystic breast mass. This case report illustrates an unusual presentation of a rare benign breast lesion. The clinical, radiographic, and pathologic features of this disease process are discussed; the literature is reviewed; and management options are discussed.

Case Report

A 39 year old Micronesian female presented to medical attention with a 2 year history of spontaneous bloody nipple discharge from the right breast. This was associated with a progressively enlarging breast mass. The patient had undergone a previous central duct excision of the ipsilateral nipple for bloody discharge 10 years prior to this presentation. Pathology at that time was consistent with an intraductal papilloma.

Physical examination was remarkable for markedly asymmetric breasts. Within the right breast was a large, nontender, well-demarcated multilobular mass occupying primarily the retroareolar and medial quadrants (fig 1). Bloody nipple discharge was noted emanating from multiple ducts. The opposite breast was normal to palpation. There was no axillary, cervical, or supraclavicular adenopathy. Mammogram demonstrated multiple well-circumscribed soft tissue masses, the largest of which measured 7cm (fig 2). A needle aspiration was performed with 800cc of serosanguinous fluid obtained. This resulted in only partial resolution of the cystic mass, and within 36 hours most of the fluid had reaccumulated. Cytology of the aspirated fluid revealed monotonous benign-appearing ductal epithelial cells with several clusters of cells arranged in a papillary configuration consistent with a papillary lesion. No atypical cells were noted. Further imaging with ultrasound and MRI was performed. Ultrasound revealed multiple complex cystic masses with internal echoes and frond-like projections extending into the cyst cavity . MRI demonstrated multiple large complex cysts with fluid-fluid levels of low signal intensity on T1 weighted images. Within these complex cysts were frond-like projections peripherally that enhanced rapidly after gadolinium (fig 3).

Because of the size of the breast masses relative to the patient's breast size and the multiplicity of the lesions, simple mastectomy was recommended; the patient refused, however, opting instead for local excision. Pathologic examination revealed gross and microscopic changes consistent with a benign intraductal papilloma (fig 5,6). Multiple cysts were noted ranging in size from several millimeters to 11cm. No additional proliferative changes were noted in the adjacent breast tissue, nor was there any evidence of in-situ or invasive carcinoma. The patient received no additional therapy.

Figure 1.— Large, nontender, well-demarcated multilobular mass occupying primarily the retroareolar and medial quadrants.

Figure 2.— Mammogram demonstrating multiple well-circumscribed soft tissue masses, the largest of which measures 7cm.

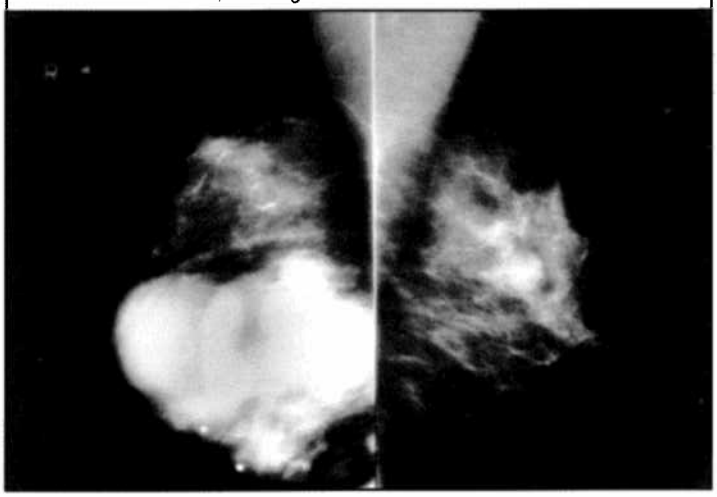


Figure 3.— MRI T1 weighted image (post gadolinium)- demonstrates multiple complex cysts with an enhancing internal frond-like projection consistent with an intraductal papilloma.

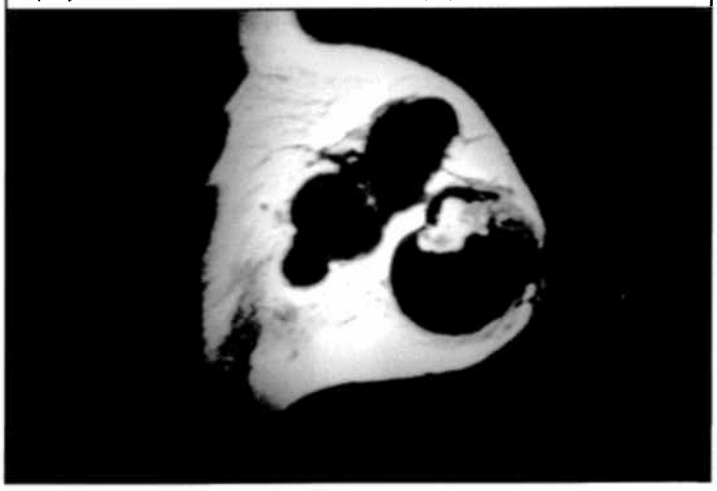


Figure 4.— Gross specimen showing large papilloma within the sectioned cyst.

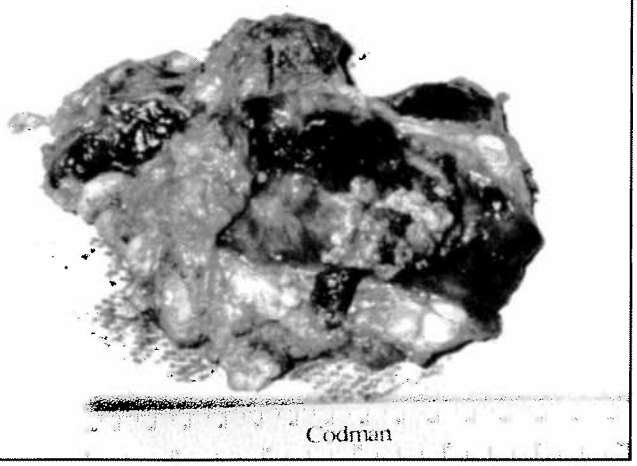
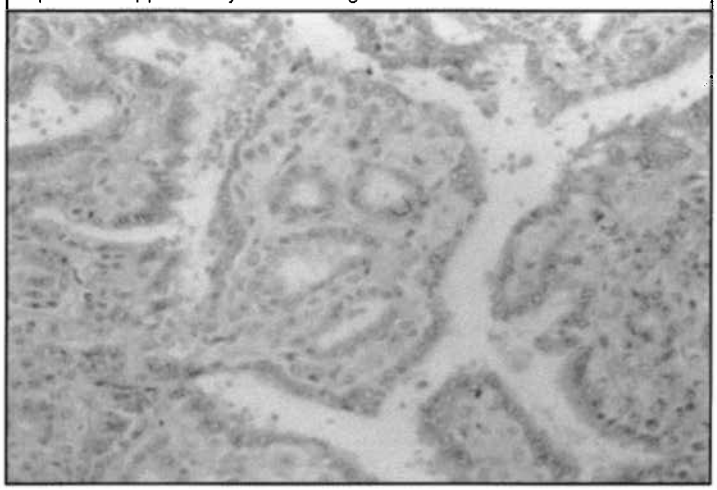


Figure 5.— Histology showing a papillary, arborescent growth pattern supported by a branching fibrovascular stalk.



Discussion

Papillary lesions of the breast are rare and make up less than 10% of all benign breast pathology. Included are solitary and multiple papillomas. Although each of these is a distinct entity that exhibits different clinical behavior, they share the common pathologic feature of a papillary, arborescent growth pattern supported by a branching fibrovascular stalk upon which a benign epithelium resides.[1-4] As Tavassoli notes, the most important task of the pathologist in assessing a papillary lesion of the breast is to determine whether it is benign or malignant (papillary carcinoma). The single most important distinguishing feature is the presence or absence of a relatively uniform myoepithelial cell layer in the proliferating, papillary intraluminal component of the lesion. Furthermore, their location or site of origin—central versus peripheral—are associated with differences in clinical behavior.[3]

Solitary intraductal papilloma is the most common benign papillary lesion. It is typically seen in mid-life with a mean age between 45 and 50 years old. As the name implies, it is a solitary proliferation of benign ductal epithelium that is usually <5mm, is rarely palpable, rarely bilateral, and typically involves a single portion of a dilated subareolar lactiferous duct. For this reason up to 90% of these lesions are associated with spontaneous nipple discharge, which may be intermittent in nature.[5-8] The character of the discharge may be serous, serosanguinous, or frankly bloody.[9, 10] If palpable, the perceived mass noted on physical examination is often the dilated duct and surrounding reaction.[6] Because of their small size, intraductal papillomas may not be visible on mammography; however, when seen they may appear as a small mass or calcifications.[8] Histologically, they are characterized by the formation of epithelial fronds on a branching fibrovascular supporting structure or pedicle attached to the duct wall.[3] There may be associated areas of sclerosis, hyperplasia, and infarction with the involved duct typically being dilated or cystic. Isolated cases of large solitary papillary tumors have been reported. Haagensen reported on a 13 cm solitary intraductal papiloma that was initially misdiagnosed as a carcinoma, and treated with mastectomy.[7] Likewise, Roy in 1985 described a case in which a simple mastectomy was performed for a 15 cm breast mass thought to be a cystosarcoma phylloides. Pathologic evaluation revealed a 15x 13x11 cm multiloculated cyst containing approximately 440 cc of bloody fluid. Contained within the cavity was a 4 x 3.5 cm friable tumor mass close to the areola and two smaller 5mm masses. Histologically, these tumors were consistent with solitary intraductal papillomas.[11]

The risk of developing breast cancer within a solitary intraductal papilloma is arguably low or nonexistent. The papilloma is probably a marker of proliferative breast epithelium and is not premalignant itself. Any increased risk of cancer is, therefore, most likely related to the degree of associated atypical hyperplastic epithelium within the papilloma or in the surrounding tissue where the papilloma arises.[5, 12-17] As demonstrated by Page et al, if atypical hyperplasia is found within the papilloma, the risk of breast cancer development increases to perhaps 1.6 times that for papillomas without atypical hyperplasia. Papillomas associated with nonhyperplastic breast epithelium carry a very low risk of developing subsequent cancer.[18] As Carter notes in his review, as the epithelium around the papilloma becomes more hyperplastic, the risk increases.[5] Conservative surgical therapy is currently recommended for solitary intraductal papillomas.

Multiple intraductal papillomas, also referred to as peripheral papillomas, are less common then the solitary intraductal papilloma.[10, 19] These lesions tend to occur in younger patients, typically form small palpable masses, and have a tendency for bilaterally. In Haagensen's series[10], the average size was 2.8cm. Because they involve mammary ducts within the peripheral sectors of the breast, they are associated with spontaneous nipple discharge in less than 20% of cases. On mammogram, they appear as well circumscribed masses with or without associated calcifications.[8] Histologically, multiple intraductal papillomas share the same basic microscopic structure as the solitary intraductal papilloma but are much more extensive resulting from involvement of multiple foci of a single duct or involving multiple duct systems. They arise in the terminal duct lobular unit and may manifest prominent hyperplasia of the epithelium and myoepithelium. These lesions may also be associated with intraductal hyperplasia, with or without atypia, in adjacent ducts.[1, 3, 6, 10]

Unlike intraductal papilloma, multiple intraductal papillomas are associated with an increased risk of developing cancer. This risk

may be as high as 38%. The breast cancer may coexist with the papilloma or develop subsequent to its excision.[5,14,17,19,20,21] Although cancers may arise within the papilloma, the general consensus is that the cancers arise within the adjacent hyperplastic epithelium. Current treatment recommendations include breast conservation with complete local excision and lifelong follow-up. The local recurrence rates after resection may be as high as 24%.[22]

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"Letter to the Editor," continued from p. 56

impossible. I guess she's come into an equilibrium with the parasites. Perhaps they are a penance that she is willing to bear.

But in her drab, foreboding world there are now tulips, and the love they stand for will last far longer that their ephemeral blooms. I recognized now that these blooms are more important that all my insights and groping theories. The tulips came from the heart of a caring person as a gift to one in pain; and that is far more of an anodyne than by insight-oriented therapy or mind-numbing drugs. If there is to be a cure for Mrs. M. and so many more like her, it is more apt to come from another's heart, from a random act of kindness, than from some physician's head.

The question is, can this be taught? Or is it innate, a gift of genes and nurture. Sadly, those who enter medical school with this aptitude often lose it in the "educational" process.\

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Editor's Note:
David J. Elpern, MD majored in comparative Literature at Columbia College and earned his Medical Degree at New York University School of Medicine in 1970. He was in general practice for four years before completing his dermatology residency at Johns Hopkins. Many readers will remember David when he practiced dermatology on the island of Kauai and was the Director of the Kauai Skin Cancer Registry.

For more than 20 years, David has had a special interest in medical education. He has organized an annual national Continuing Medical Education course in Dermatology "Hot Spots in Dermatology" as well as symposium on the medical humanities for the past 10 years. The next "Hot Spots" is planned for August 2001 on the Big Island of Hawaii. He is also organizing a conference to be held in Cuba in January 2002. David can be contacted via fax at (413) 458-4224 and on the Web at kauai@bcn.net.

Until there's a cure, there's the American Diabetes Association.